



## Synthesis, Characterization, Spectral Studies, Biocidal Activities of Fe (II) and Cu (II) complexes of Azo dye Ligand Derived from Sulfamethoxazole and Substituted p-Cresol

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### ABSTRACT

P-Cresyl acetate (I) has been prepared by acetylation of p-Cresol. Fries migration of (I) yields 2-Acetyl-4-methyl phenol (II). Clemmensen's reduction of (II) yields 2-Ethyl-4-methyl phenol (III). Diazonium salt (IV) prepared by diazotization of sulfamethoxazole. Azo dye ligand 3-ethyl-2-hydroxy-5-methyl-4'-(5"-methyl-oxazole-3"-yl) amino sulphonyl azobenzene (V) has been prepared by coupling of 2-Ethyl-4-methyl phenol (III) with Diazonium salt (IV) at 0-5 °C. By refluxing alcoholic solution of ligand with aqueous solution of metal salts yields azo dye ligand complexes (VI) of  $ML_2(H_2O)_2$  or  $ML_2$  type. They were characterized by elemental analysis, absorption spectra, conductivity measurement, molecular weight determination and magnetic susceptibility measurements. The ligand as well as the metal complex has been screened for their antimicrobial activity against a number of micro organisms.

**Key words:** Synthesis, ligand, metal complexes, characterization, antimicrobial activity.

### INTRODUCTION

In the last few years, chemists have taken a growing interest in the synthesis and physico-chemical studies of first row transition metal complexes with a number of azo dye ligand<sup>1-2</sup>. Metal complexes of azo dye ligand have played a central role in the development of co-ordination chemistry. The systematic synthetic study of azo dye ligand complexes was commenced by Farben Fabriken Bayer<sup>3</sup> and Kraska, Jan; Czajkowski, Wojciech<sup>4</sup>. A survey of the literature reveals that much work has been done on the synthesis and physico-chemical studies of metal complexes<sup>5-8</sup> of number of azo dye ligand.

Azo dyes (V) of sulfa drugs are well known for their antiseptic activity<sup>9-9</sup> and some are useful as chemotherapeutic agents<sup>10</sup>. Transition metals like Fe, Co, Ag, Au, Cu and Ni have long been used in medicine. A large number of metal sulphonamide complexes are found to be more potent than the parent sulphonamides<sup>11-12</sup>. In view of getting potent therapeutic agents present paper reports the synthesis of titled compounds [V, VI (a-b)].

The titled compounds have been synthesized by the reaction of alcoholic solution of 3-ethyl-2-hydroxy-5-methyl-4'-(5"-methyl-oxazole-3"-yl) amino sulphonyl azobenzene (ligand) with aqueous solution of Fe(II) & Cu(II) metal salts. The

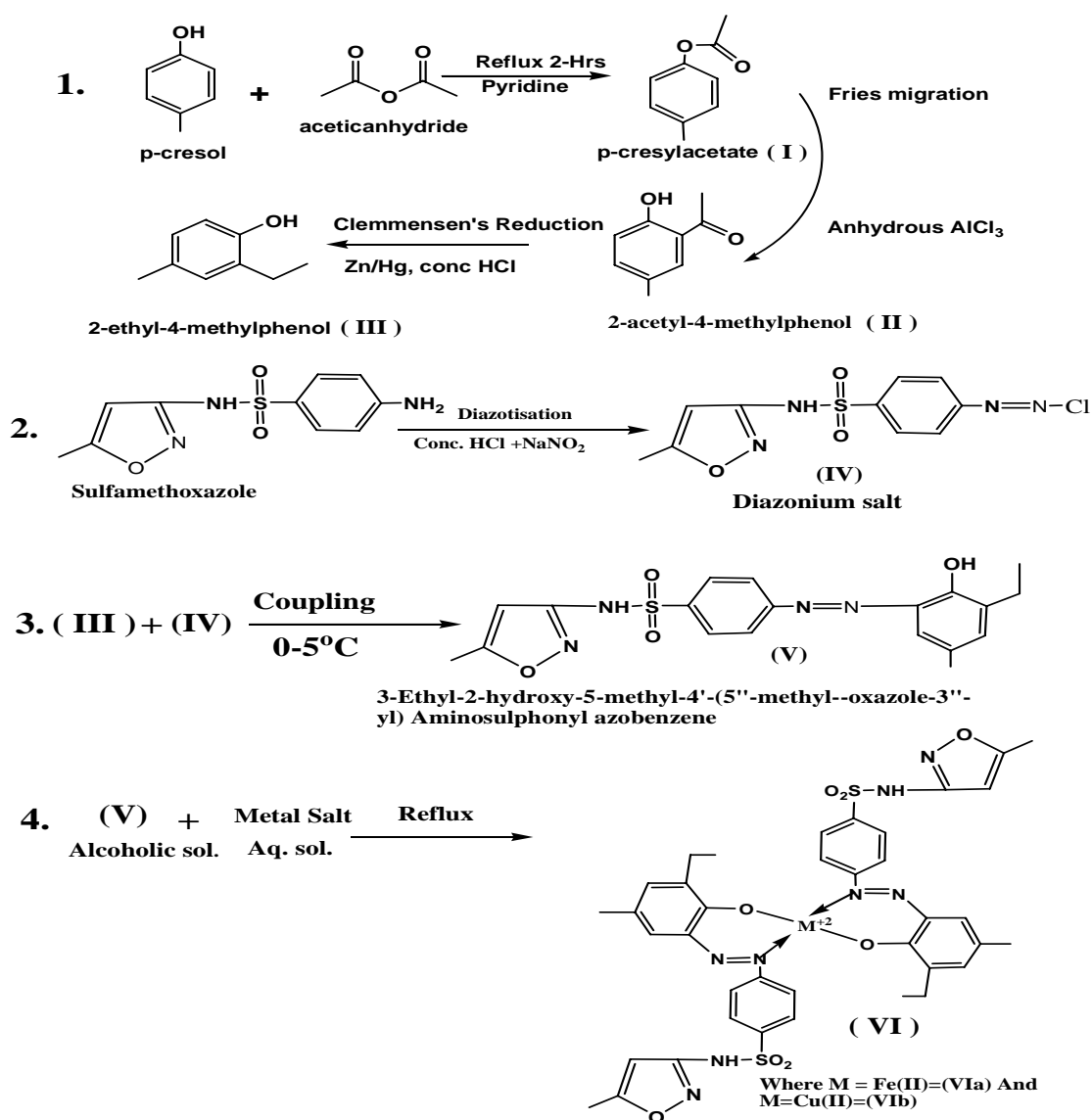
later of ligand have been synthesized by coupling of diazotized sulfamethoxazole with 2-ethyl-4-methyl phenol. 2-ethyl-4-methyl phenol has been synthesized by the clemmensen reduction<sup>13-14</sup> (Zn/Hg, Conc.) on 2-acetyl-4-methyl phenol. The later was synthesized by the fries migration<sup>15</sup> on P-cresyl acetate have been synthesized by the acetylation<sup>16</sup> of P-cresol with acetic anhydride in presence of pyridine.

to have antimicrobial activity comparable to that of standard drugs, viz. sulfamethoxazole, and sulfadiazine. The product have also been characterized by elemental analysis, absorption spectra, conductivity measurements, molecular weight determination, magnetic susceptibility measurements and stepwise stability constants by P<sup>H</sup> metric method. By using the results of above study, structure of metal complex is proposed.

The products have been evaluated for antimicrobial activity. Some compounds are found

### Material and methodlogy

Synthesis of ligand and metal complexes.



Scheme

## RESULTS AND DISCUSSION

### IR Spectral data of the ligand

IR (KBr)  $\text{cm}^{-1}$ : 3432 (N-H str. Sym. & O-H str.), 3080 (= C-H str.), 2969 (C-H str.- $\text{CH}_3$ ), 2915 (C-H str.- $\text{CH}_2$ ), 2860 (C-H str.sym.), 1614(-N=N-str. & N-H def.), 1580 (-C=C str.), 1467 (oxazole ring str.), 1417 (C-H def.asym.,-N=N- Str.), 1398 (O-H def. & C-H def.sym.), 1341 (S=O str.asym.), 1264 (C-H i.p. def.disub.benzene), 1177 (S=O str.sym.), 1140 (C-H i.p. oxazol), 1034 (ring skeletal oxazol), 900 (C-H o.o.p. oxazol), 755 (N-H wag.).

### NMR Spectral data of the ligand.

$^1\text{H}$  NMR ( $\text{CDCl}_3$ ): 1.21-1.25  $\delta$ (3H,t,- $\text{CH}_2$ - $\text{CH}_3$ ), 2.34-2.38  $\delta$ (6H, 2 x s, 2 X - $\text{CH}_3$ ), 2.64-2.71  $\delta$ (2H,q, - $\text{CH}_2$ - $\text{CH}_3$ ), 6.28  $\delta$ (1H,s, =  $\text{CH}$  oxazole ring), 7.11  $\delta$  (1H, s, Ar-H), 7.54  $\delta$  (1H, s, Ar-H), 7.86-7.89  $\delta$  (2H, d, Ar-H), 7.96-7.98  $\delta$  (2H, d, Ar-H), 12.86 (1H,s,Ar-OH).

### Mass Spectra

(m/z): 401 ( $\text{M}^+$ ), 309, 287, 266, 239, 207, 154, 135, 120, 105, 91, 77, 69, 55, 41.

### Absorption Spectra

$\lambda_{\text{max}}$  (nm): 232, 323, 362, 412.  
 $\log \epsilon$ : 4.3456, 4.2735, 4.3237, 4.1455.

### Antimicrobial Activity

The testing were carried out by cup-plate method at a concentration of 50  $\mu\text{g}$  using gram positive bacteria as *B. megaterium* and *B. subtilis* and gram negative bacteria as *E. coli*. And *P. fluorescens* and fungi as *A. awamori* and *A. niger*. Most of the compounds were moderately active against different strains of bacteria and fungi. However, comparatively significant was observed in compounds (along with zone of inhibition in mm) having azodye ligand (V)-(18), Fe (II) complex (VIa)-(22), Cu (II) complex (VIb)-(16) against *B. mega*, azodye ligand (V)-(14), Fe (II) complex (VIa)-(21), Cu (II) complex (VIb)-(17) against *B. subtilis*, azodye ligand (V)-(16), Fe (II) complex (VIa)-(17), Cu (II) complex (VIb)-(22) against *E. coli*, azodye ligand (V)-(18), Fe (II) complex (VIa)-(18), Cu (II) complex (VIb)-(18) against *A. arogens*, azodye ligand (V)-(17), Fe (II) complex (VIa)-(19), Cu (II) complex (VIb)-(18) against *A. awamori*, azodye ligand (V)-(19), Fe (II) complex (VIa)-(18),

Cu (II) complex (VIb)-(19) against *A. niger*

### Physical method

Molar conductivities of  $10^{-3}$  M solutions of the complexes in DMF were measured on a Toshniwal conductivity bridge, using a dip type cell at room temperature. Magnetic susceptibilities were measured at room temperature on a Gouy balance using mercury (II) tetrathiocyanato cobaltate (II) as the calibrant. IR spectra were obtained using KBr disc on NICOLET MEGNA-IR 550 SERIES II.

### $\text{P}^{\text{H}}$ -metric measurements

For the determination of stepwise stability constants an expanded scale systronic  $\text{P}^{\text{H}}$  meter with accuracy  $\pm 0.02$  units was employed. All experiments were carried out at  $30 \pm 0.2$   $^{\circ}\text{C}$  and temperature was mentioned constant using thermostat. The three sets acid, acid + ligand, acid + ligand + metal were prepared.

In each case total volume was made up to 40 ml by adding required amount of double distilled water or purified dioxane as the case may be. The ionic strength was maintained by adding appropriate amount of sodium nitrate (0.01M) and mixtures were titrated with standard NaOH solution. A modified form of Irving-Rosstti<sup>17</sup> titration technique was used for calculating the stability constants. The  $\text{P}^{\text{H}}$  meter was calibrated with aqueous buffers. In the calculations for pL the pH meter reading 'B' was used instead of converting it to true pH value (Corresponding to aqueous medium). The use of pH meter reading 'B' instead of true pH values did not make any differences<sup>18-19</sup> in the calculation of free ligand concentration and was usually valid for water dioxane media.

### Conductance measurements

Molar conductance values of all the complex in  $10^{-3}$  M DMF solutions are given in Table-1. These values are consistent with the non-electrolytic<sup>20</sup> nature of this complex.

### Magnetic measurements

The observed magnetic moments of the resulting complex are given in Table-1. This value shows that Fe (II) complex is diamagnetic and Cu (II) complex is paramagnetic nature with one unpaired<sup>21-22</sup> electron.

Table 1: Some Physical Properties of metal complexes

Comp.	Molecular weight Found/ (Req.)	Elemental analysis % found/(calculated)				Conductivity (Mohs.cm <sup>2</sup> mole <sup>-1</sup> )	$\mu_{\text{eff.}}$ B.M.
		M	C	H	N		
Fe(C <sub>19</sub> H <sub>19</sub> O <sub>4</sub> N <sub>4</sub> S) <sub>2</sub> (H <sub>2</sub> O)	879.25 (889.85)	6.28 (6.31)	51.24 (51.27)	4.72 (4.75)	12.59 (12.63)	12.5	Diamag
Cu (C <sub>19</sub> H <sub>19</sub> O <sub>4</sub> N <sub>4</sub> S) <sub>2</sub>	854.46 (861.54)	7.37 (7.41)	52.93 (52.96)	4.41 (4.45)	13.00 (13.03)	8.6	2.08

Table 2: Stepwise stability constants of metal complexes of 3-ethyl-2-hydroxy-5-methyl-4'-(5"-methyl-oxazol-3"-yl)-amino-sulphonyl azobenzene in (60: 40) Dioxane: Water,  $\mu = 0.1\text{M}$ , Temp  $30 \pm 0.2^\circ\text{C}$ .

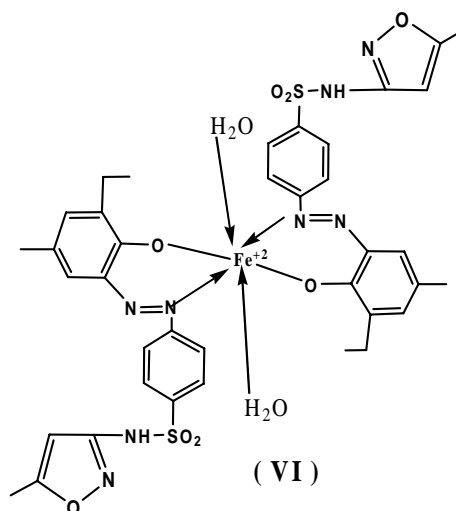
Ligand	$\log K_1^H$	$\log K_2^H$	$\log B_2^H$
C <sub>19</sub> H <sub>20</sub> O <sub>4</sub> N <sub>4</sub> S	10.622	3.703	14.365
Complex	$\log K_1$	$\log K_2$	$\log B_2$
Fe (C <sub>19</sub> H <sub>19</sub> O <sub>4</sub> N <sub>4</sub> S) <sub>2</sub> ·(H <sub>2</sub> O) <sub>2</sub>	5.6828	3.2211	8.9039
Cu (C <sub>19</sub> H <sub>19</sub> O <sub>4</sub> N <sub>4</sub> S) <sub>2</sub>	8.2522	5.7024	13.9546

### UV and Visible spectra

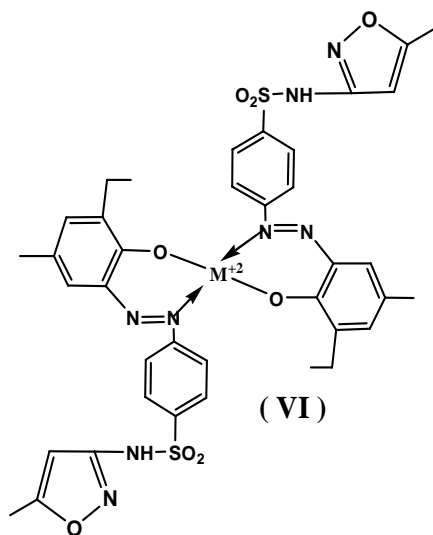
The spectra of Fe(II) complex show a very diffused band at 788 nm showing octahedral structure. The Mossbauer spectra shows two symmetrical bands indicating distorted octahedral geometry which is support of the fact that there are two water molecules and two ligands molecules attached with Fe<sup>II</sup> ion. The spectra of copper (II) complex (D<sub>4</sub>h) three Absorption bands are expected corresponding to  ${}^2B_{1g} \rightarrow {}^2A_{1g}$ ,  ${}^2B_{1g} \rightarrow {}^2B_{2g}$  and  ${}^2B_{1g} \rightarrow {}^2E_g$ . In the present case, only two absorption bands are obtained at  $\lambda_{\text{max}}$  635nm & 770nm and are attributed to the transition  ${}^2B_{1g} \rightarrow {}^2E_g$ , and  ${}^2B_{1g} \rightarrow {}^2B_{2g}$  respectively. The  ${}^2B_{1g} \rightarrow {}^2A_{1g}$  band would have overlapped with  ${}^2B_{1g} \rightarrow {}^2B_{2g}$  band and so it could not be seen in the spectra. However, their special data support the square planner geometry of the copper complex.

From these observations it is concluded the iron (II) complex is distorted octahedral in nature

where as copper (II) is square planner. The structure of iron (II) complex and copper (II) complex are as under.



**M=Fe(II)=(VIa)**



M=Cu(II)=(VIb)

### Potentiometric study

The P<sup>H</sup> metric studies of the metal complex show the n values as 1.80 and 1.69 for Fe (II) and Cu (II) respectively, indicating two ligands per metal ion, the stepwise stability constants (Table-2) follow the Irving-Williams order.

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